REMARKS/ARGUMENTS

Claims 41-82, 84 and 85 are pending. Applicants have amended the claims to correct clerical errors and to recite more clearly and distinctly that which they consider the invention. It is respectfully submitted that the amendments are fully supported by the application as originally filed and do not raise any issues of new matter. Entry and favorable reconsideration of the claims are earnestly solicited.

Sequence Compliance and Claim Objections

Applicants thank the examiner for, and have complied with, the kind suggestion with regard to the legend of Figure 6, thereby obviating this issue.

Applicants have also amended claims 61 and 77, overcoming their objections.

Claim Rejections under 35 U.S.C. § 112 ¶ 2

In order to expedite prosecution and advance this application to allowance, applicants have amended relevant claims which amendments are believed to have overcome all claim rejections for alleged indefiniteness. Specifically, the recitation of "a gene or a part there of ... having p450 activity" has been changed to a polynucleotide ... having a p450 activity of converting acetaminophen to a cytotoxic molecule." With regard to Claims 44-46 and 66-68, the recitation of "viral-based vector" has been changed to simply a "viral vector." It is respectfully submitted that the meaning of "viral vector" is clear to a person ordinarily skilled in the art of genetic engineering. Claim 46

has been further amended to remove the recitation of "a vector comprising a vector" and to recite that the vector is derived from one of the recited viruses. Claim 48 has been amended to remove the recitation of an "effective part" of a promoter.

The Office Action objects to the use of the term "substantially" in Claims 64 and 67-68. Applicants respectfully submit that a rejection of the claims on this basis is improper and request that the examiner reconsider. Tissue- or developmental stage-specific promoters are well known in the art. It is equally well known, however, the specificity of such promoters varies because many of these promoters are leaky to some degree. If a promoter directs gene expression predominantly in a particular tissue, or during a particular developmental stage, this promoter will be called a promoter specific for that tissue or developmental stage. In the context, the term "substantially" is perfectly permissible and its meaning clear to a person of ordinary skills in the art. As indicated in MPEP § 2173.05(b)(D), several CCPA or Federal Circuit court cases have determined that the term "substantially" is permissible in patent claims.

Finally, Claims 68 and 72 have been amended to remedy the lack of antecedent problem.

Claim Rejections under 35 U.S.C. § 112 ¶ 1

Lack of Written Description

The Office Action rejected all pending claims for alleged lack of written description, asserting that the specification, while provide examples of cDNAs

that encode a polypeptide having a p450 activity, does not provide adequate written description for a "gene or a part" thereof. It is respectfully submitted that rejection has been rendered moot by the claim amendment, which replaced the recitation of "a gene or a part thereof" with "a polynucleotide," and which also specified the activity of the encoded polypeptide by the polynucleotide.

Lack of Enablement

A substantial part of the Office Action was devoted to the analysis behind the rejection of all claims for alleged lack of enablement. This lengthy discourse, however, can be summarized into two points: First, the recitation of a "gene" in the claims render the claims non-enabled. This, as discussed above, has been obviated by the claim amendment. Secondly, the Office Action asserts that there is no *in vivo* data showing that the method would actually work in mammals, and that this problem is exacerbated by the fact that gene therapy, which so far has seen no clinical success, is involved in the claimed method and compositions. Applicants respectfully traverse this rejection and submit that the Office Action applied an incorrect legal standard.

It is apparent that the Office Action does not assert that the actual performance of the claimed method, or the make of the claimed composition, requires undue experimentation (the classical lack of enablement situation). Rather, the Office Action doubts that the claimed method or composition would actually or credibly accomplish the intended therapeutic objectives. In other words, this is a situation where the lack of enablement rejection is actually based

on the assertion that the claimed invention has no patentable or "credible" utility.

It is, of course, well-established that inventions asserted to have utility in the treatment of human or animal disorders are subject to the same legal requirements for utility as inventions in any other field of technology. *In re Chilowsky*, 229 F.2d 457, 461-2, 108 USPQ 321, 325 (CCPA 1956). Furthermore, courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use satisfies the utility requirement. As the Court of Customs and Patent Appeals held:

> Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility.

Nelson v. Bowler, 626 F.2d 853, 856, 206 USPQ 881, 883 (CCPA 1980).

Similarly, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. The Federal Circuit, in *Cross v. Iizuka*, 753 F.2d 1040, 1051, 224 USPQ 739, 747-48 (Fed. Cir. 1985),

commented on the significance of data from *in vitro* testing that showed pharmacological activity:

> We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility.

The Federal Circuit has reiterated that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs to marketed in the United States.

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. *Scott [v. Finney]*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed.Cir. 1994)]. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). To put it differently, the discussion of all the potential side effects of some of the viral vectors used in gene therapy in the Office Action is irrelevant for the legal analysis of enablement. Even if a test animal dies as a consequence of the claimed treatment method, as long as the cancer symptoms is abated by the treatment, under the patent law, the claimed method is both enabled and useful.

Given the case law such as those discussed above, the MPEP specifically states that "Office personnel should not construe 35 U.S.C. 101, under the logic of 'practical' utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or fully effective drug for humans." MPEP § 2107.01(III).

The MPEP further explicitly states that "these general principles are equally applicable to situations where a process for treating a human or animal disorder is the claimed subject matter". *Id.*

The Office Action relies on discussion in the literature of difficulties of gene therapy, all of which are in the context of a clinical effectiveness or usefulness. The scientific literature, on the other hand, also contain success stories of gene therapy, albeit some of them are in an early testing stage or in animal tests only, or the effective/successful examples may not be statistically significant to be practically a clinical success, or that severe side effects also exist. Nevertheless, these successes, although limited would be evidence of "enablement and utility" under the patent law.

Therefore, applying the proper legal standard, it is clear that the claimed compositions and methods have credible and patentable utility. In addition, as discussed above, there is no question that the claimed method can be made/used by an ordinarily skilled artisan without any need of undue experimentation. Accordingly, the claims satisfy the enablement requirements under 35 U.S.C. §

112, ¶ 1, and the claim rejections on this ground are improper and should be withdrawn.

In conclusion, applicants respectfully submit that in view of the above claim amendments and arguments, all claims are now in condition for allowance and earnestly solicit an early indication from the Examiner to that effect.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #01033149927).

Respectfully submitted,

May 25, 2004

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